

Serum IgE Levels : Correlation with Skin Test Reactivity in Thai Adults with Respiratory Allergy

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Immunoglobulin E was identified by Ishizaka and his co-workers in 1966.¹ It is believed to be the class of antibody responsible for the signs and symptoms found among patients with allergic diseases, particularly those with immediate type of hypersensitivity.² It is normally present in human serum in very small amounts and requires extremely sensitive methods for detection and quantitation. High serum IgE levels can be demonstrated in many allergic diseases, such as bronchial asthma, allergic rhinitis, atopic dermatitis, urticaria and allergic aspergillosis.³⁻⁹

Allergy skin testing has been a standard tool in the clinical evaluation of allergy for many years. However, skin tests cannot be performed in infants, patients with some skin diseases, patients with histories of severe allergy and in patients who have been taking drugs that may disturb the results of skin testing. Consequently total IgE and specific IgE levels are used in order to avoid those problems. Serum IgE and skin test reactivity are generally considered to be interrelated variables associated with atopy. This close relationship

SUMMARY A history of respiratory allergic disorders was obtained in 68 patients. Allergic skin testing was performed with measurement of total IgE by enzyme immunoassay (EIA). The mean level of total IgE from the control group of 13 healthy adults with no history of allergic diseases was 24.7 IU per ml. The average serum IgE level among the allergic patients with positive skin tests was 97.6 IU per ml and it was significantly higher than that of the controls ($p < 0.005$). It was also found that the positive skin test patients had significantly a higher mean serum IgE level than that of patients with negative skin test results (97.6 vs 33.6 IU per ml, $p < 0.01$). Since 73.2% of the allergic patients with positive skin tests had serum IgE levels over 45 IU per ml while only 23.1% of the control group had IgE levels exceeding this figure, we consider that a patient with clinical symptoms and a serum IgE level over 45 IU per ml is likely to be suffering from allergic disease.

between allergy skin test reactivity and serum IgE level in allergic patients and in the normal population has been reported.¹⁰⁻¹⁴ However, no studies have been done among Thai patients, particularly in adults. Therefore, the purpose of this study was to compare the serum IgE levels in Thai adults with respiratory allergy with those of normal controls and to investigate the relationship between skin test reactivity and serum IgE levels in these allergic patients.

MATERIALS AND METHODS

Study subjects

Serum samples were obtained from those who attended the out patient allergy clinic at the Depart-

ment of Medicine, Ramathibodi Hospital, Mahidol University. The test group consisted of 35 bronchial asthmatic patients (age range 18-54 years, mean 34.2 years), 33 allergic rhinitis patients (age range 15-62 years, mean 32.9 years) and 13 healthy subjects with no history nor clinical evidence of allergy (age range 22-36 years, mean 31 years). The diagnostic criteria for asthma and allergic rhinitis

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were based on those described by Border *et al.*¹⁵ Each patient was instructed not to take any antihistamines or related drugs for 72 hours prior to skin testing. In the control group, we determined only serum IgE levels but in the patient group we did both serum IgE levels and skin testing.

Antigens

A panel of 23 common local allergens was prepared for the evaluation of skin testing. The glycerin-preserved antigen (Greer Laboratories) included the grass pollen group (Bermuda, Lambs quarter, Kochia, Cocklebur, Acacia, Corn smut), the mold group (*Candida*, *Alternaria*, *Aspergillus*, *Fusarium*, *Penicillium* mix), the perennial environmental group (house dust, *D-farinae*), the feather group (pigeon, feather mix), the animal dander group (cat, dog) and miscellaneous (kapok, silk, cockroach, orris root, pyrethum). These glycerin-preserved allergens for prick testing were administered in 1:20 w/v dilutions, while 0.4% phenol preserved aqueous solutions for intradermal testing were prepared in standard 1:1,000 w/v dilutions.

Skin tests

Two different methods¹⁶ (prick test and intradermal test) were performed by a trained nurse. Prick tests were applied on the volar surface of the forearm, using a scarifying lancet in all allergic patients. Intradermal tests were performed on the upper and outer aspect of the arm, using a 1 ml tuberculin syringe and

a 27-gauge needle in patients who had negative reactions by prick testing. A buffered diluent was administered as a negative control and histamine 1% and 0.01% in a base solution were used as positive controls for the prick and intradermal tests, respectively. In this study, all antigens were from the same lots and skin tests were performed by the same nurse. Wheal reactions were recorded at 20 min, and were graded according to King and Norman.¹⁷ The subjects with negative responses to all antigens by both methods were considered to be skin test negative, whereas those with 1+ or more reactions to any allergen by either method were grouped as skin test positive patients.

Serum IgE determination

Venous blood samples were drawn at the time of skin test examination and the sera were kept frozen at -20°C until analysis. Serum IgE levels were determined by using a commercially available kit (Enzygost-IgE, Calbiochem Berhing Corp.). This enzyme immunoassay for human IgE utilizes anti-IgE antibody which was previously immobilized on plastic test tubes (solid phase). The IgE in the serum to be assayed will be bound by this solid phase coupled antibody. After washing, the coated tubes are incubated with peroxidase-conjugated antibody to human IgE which binds to the IgE present. The total amount of enzyme labeled anti-IgE bound to the coated tube is directly related to the amount of

IgE present and is converted to international units (IU) by means of a standard curve.

Statistical analysis

The serum IgE levels were converted to the \log_{10} for computation and the antilog or geometric mean values were displayed in the figures and tables. Unpaired student's *t* test was used to determine the differences between groups which were considered significant if $p < 0.05$.

RESULTS

Skin tests were positive in 82.4% of allergic patients ($n=68$) as shown in Table 1. When the allergic patients were divided into two groups, asthmatic patients had a higher percentage of skin test positivity than rhinitis patients (91.4% vs 72.7%).

Serum IgE levels in the allergic patients and the non-allergic controls are presented in Fig. 1. Allergic patients had a wide range of serum IgE levels (10.5-570 IU per ml). The geometric mean serum IgE level of the allergic asthma patients was significantly greater than that of the allergic rhinitis group (111.4 vs 57.6 IU per ml, $p < 0.05$) and that of the normal controls (111.4 vs 24.7 IU per ml, $p < 0.005$). There was no significant difference between the geometric mean serum IgE level of the allergic rhinitis patients and the normal controls (57.6 vs 24.7 IU per ml, $p=0.06$).

Table 1. Skin test results in allergic patients.

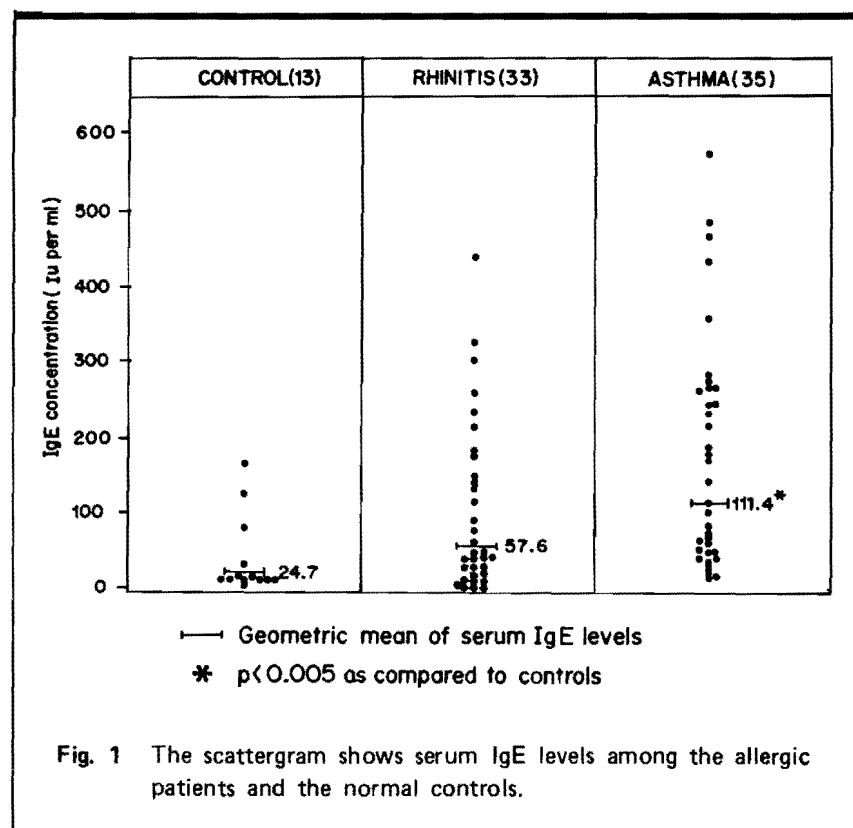
Subjects	Number	Positive skin test		Negative skin test	
		N	%	N	%
Allergic asthma	35	32	91.4	3	8.6
Allergic rhinitis	33	24	72.7	9	27.3
Total allergic patients	68	56	82.4	12	17.6

Table 2. Percentages of patients in each category with serum IgE greater and less than 45 IU per ml.

Subjects	Total	IgE ≤ 45 IU per ml		IgE > 45 IU per ml	
		N	%	N	%
Positive skin test	56	15	26.8	41	73.2
Negative skin test	12	8	66.7	4	33.3
Control	13	10	76.9	3	23.1

When we classified the allergic patients into two groups according to their skin test reactivity, we found that the geometric mean serum IgE level of the skin test positive group was significantly greater than that of the skin test negative group ($p < 0.01$) and that of the non-allergic controls ($p < 0.005$). No significant difference existed when the IgE levels from those whose skin test were negative were compared with the controls ($p = 0.68$), as shown in Fig. 2. No one in the non-allergic group or in the skin test negative group had a serum IgE level greater than 165 IU per ml.

There was a positive correlation between serum IgE levels and skin test results when the individual skin test classifications were examined ($r = 0.34$, $p = 0.005$). With each increase of skin test reactivity, more patients had a higher serum IgE level and the highest values increased. The geometric values for serum IgE in each classification showed the same correlation between increasing skin test reactivity and increased serum IgE (Fig. 3). Allergic patients with negative skin test had a geometric mean serum IgE of 33.6 IU per ml which was significantly lower than the 1+ (86.0 IU per ml, $p < 0.016$), the 2+ (94.4 IU per ml, $p < 0.014$) and the 3-4+ (107.8 IU per ml, $p < 0.011$) positive allergic patients. The results indicate that the higher the serum IgE value the greater the chance that strong skin reactions



will occur and the more likely that a state of allergy exists in the patient.

Table 2 reveals that 73.2% of the positive allergic, 33.3% of the negative allergic and 23.1% of the non-allergic controls had serum IgE more than 45 IU per ml. This may be used as an arbitrary dividing line of serum IgE level to indicate the decision on whether to proceed with skin tests. However, there is no serum IgE value that would produce

a sharply defined cut-off point between allergy and non-allergy.

DISCUSSION

Skin test and serum IgE determination are a diagnostic tool for allergic diseases. The purpose of this study was to determine the correlation between skin test reactivity, level of total serum IgE and severity of respiratory allergy in Thai adults.

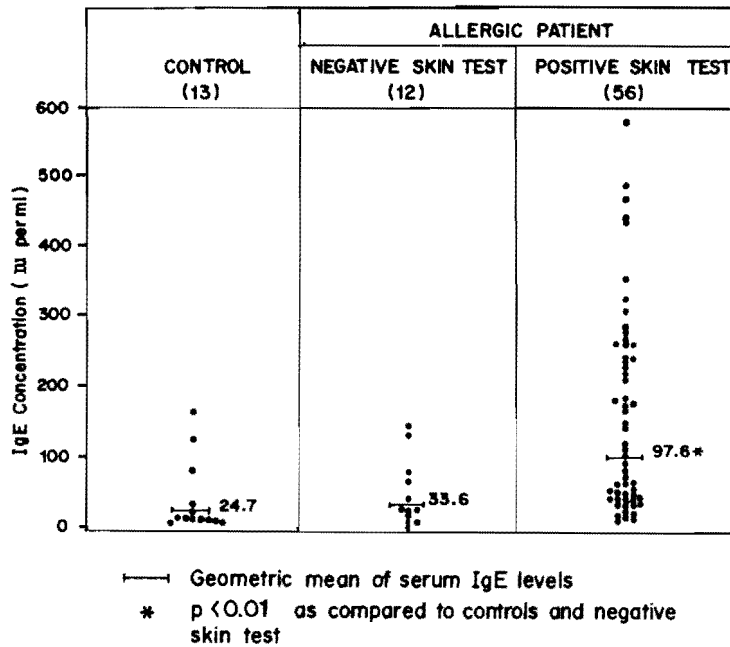


Fig. 2 The scattergram shows serum IgE levels among the allergic patients classified according to the skin test reactivity and the normal controls.

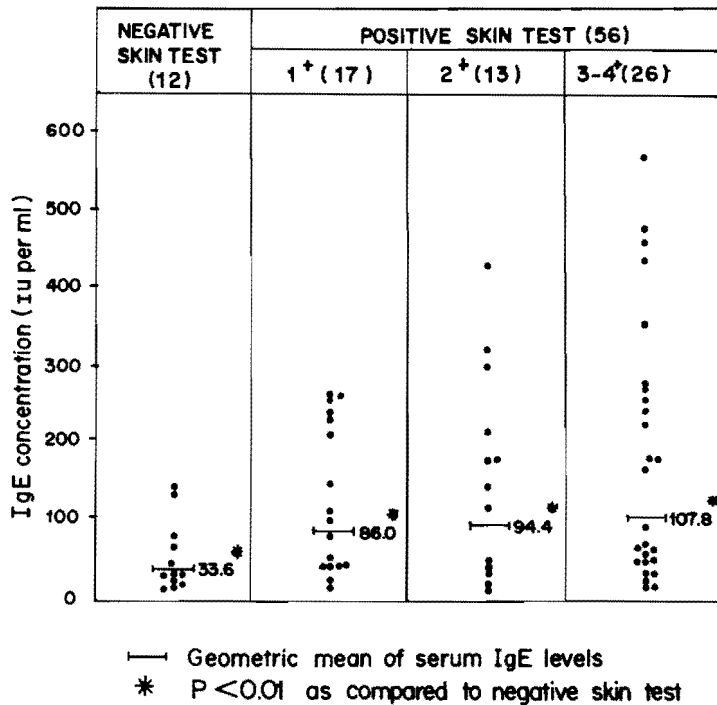


Fig. 3 The scattergram shows serum IgE levels of the allergic patients classified according to skin test reactivity.

We found that skin test positivity in allergic patients was 82.4% which was comparable to a previous study.¹⁸ Patients with asthma had a higher percentage of skin test positivity than patients with rhinitis (91.4% vs 72.7%). We did not perform skin tests in non-allergic subjects but previous study in Thai populations showed 31% positive (Prof. M. Tuchinda, personal communication). The studies in other countries similarly showed a 17-37% positivity in the normal population.^{10,19,20} Thus, the percentage of skin test positivity seem to increase according to severity of the diseases.

Measurement of serum IgE level was done by an enzyme linked immunoassay (EIA) because of its simplicity, sensitivity, cheapness and lack of radioactive label. The mean serum IgE level in 13 non-allergic controls was comparable to those measured by Dati²¹ and Nye *et al.*²² Patients with asthma had the highest mean serum IgE level (111.4 IU per ml). The level of serum IgE appeared to increase according to severity of the disease.

A distinct correlation exists between serum IgE and skin test results. When we grouped allergic patients according to their skin test reactivity, the strongly positive individuals had higher mean IgE levels. This finding confirmed those reported previously.^{11,23} It is therefore possible that serum IgE may be an influential factor in the positivity of allergic skin tests.

In conclusion, our study of serum IgE in Thai adults with respiratory allergy revealed that:

1. There is a correlation between skin test reactivity, level of serum IgE and severity of respiratory allergy. This is confirmed by the finding that asthmatic patients were 91.4% skin test positive and had mean IgE level of 111.4 IU per ml while rhinitis subjects were 72.7% positive with a mean IgE level of 57.6 IU per ml.

2. There was an increase in serum IgE with each increase in skin reactivity. Thus, skin test sensitivity bears a direct relationship with serum IgE levels. The higher the serum IgE value, the greater the chance that strong skin reactions would occur.

3. The separation of allergy from non-allergy may not be easily accomplished by determining serum IgE levels alone as there was an overlap of serum IgE levels in atopic conditions and in normal subjects. However, serum IgE level at 45 IU per ml may be used as an arbitrary guideline as to which patients should have skin tests as 73.2% of the positive allergic and only 33.3% of the negative individuals had a serum IgE higher than this level. Moreover, any patient with a serum IgE greater than 165 IU per ml should be suspected as having allergic diseases.

From the aforementioned information the measurement of serum IgE levels by the enzyme immunoassay method has, in combination with clinical examination and skin testing, proved to be a relatively simple, reliable and valuable laboratory test in the assessment of suspected allergic diseases.

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